REMARKS

Claims 5-8, 11, 12, 14-17, 19, 22-24, 29-37 and 40-50 presently appear in this case. No claims have yet been acted upon on the merits. All of the claims have been subject to a restriction requirement. Reconsideration and withdrawal of the restriction requirement and action on all of the claims now present in the case is hereby respectfully urged.

The examiner has required restriction, stating that the application contains inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. Applicants have been required in response to this action to elect a single invention to which the claims must be restricted. The examiner has cited 20 different groups which allegedly are not so linked as to form a single general inventive concept. In addition, upon the election of any of Groups I-XX further election of the patentably distinct species of (1) B1 protein and fragments thereof or (2) isoforms, analogs or derivatives of B1 is required. The examiner has required a further election of species if any of Groups IV-VIII are elected and another species election if Group VI is elected. The examiner has indicated another species election if Groups IX or XIX are elected and a further species election if Groups XIV-XVII are elected, and still another species election if Group XVIII is elected.

The examiner states that the groups lack the same or corresponding special technical feature. The examiner states that the protein is structurally distinct from the DNA and, therefore, cannot share the same special technical feature. The examiner has not alleged that the B1 protein is not novel. This restriction is respectfully traversed.

In order to be responsive, applicants hereby elect Group I, drawn to DNA, including the species of B1 protein and fragments thereof. However, this election is explicitly made with the following traversal.

For the purpose of this restriction requirement, the examiner has conceded that the B1 protein of the present invention is novel, as is the DNA encoding this protein. Therefore, the special technical feature shared by all the claims of the present case relates to the novel B1 protein and the activity thereof.

It is totally inappropriate under PCT Rule 13.1 to restrict between a protein and the DNA sequence encoding that protein, i.e., Groups I and II. The examiner's attention is invited to PCT Administrative Instructions, Annex B, Unity of Invention, Part II, Examples Concerning Unity of Invention, Example 17, which expressly states with respect to the propriety of restriction between a first claim directed to a DNA sequence and a second claim directed to the protein encoded thereby:

> Expression of the DNA sequence in a host results in production of a protein which is determined by the DNA sequence. The protein

> and the DNA sequence exhibit corresponding special technical features. Unity between claims 1 and 2 is accepted.

It is incumbent upon the examiner to follow these administrative guidelines. Therefore, Groups I and II must be combined. Accordingly, applicants elect the combination of Groups I and II.

Furthermore, the examiner's attention is invited to PCT Administrative Instructions, Annex B, Part I(e), "Combinations of Different Categories of Claims". This states:

> The method for determining unity of invention under Rule 13 shall be construed as permitting, in particular, the inclusion of any one of the following combinations of claims of different categories in the same international application:
>
> (i) In addition to an independent claim for a given product, an independent claim for a process specially adapted for the manufacture of the said product, and an independent claim for a use of the said product, ... it being understood that a process is specially adapted for the manufacture of a product if it inherently results in the product ....

Thus, in addition to the DNA or polypeptide claim, applicants are entitled to examination of a process specially adapted to the manufacture of the product as well as a claim for use of the product. Accordingly, applicants further elect the use of claim 49, which is directed to the use of either the polypeptide or the DNA. Thus, all the claims the examiner characterizes as Groups I, II, IV and V are clearly directed to a single invention in accordance with the PCT

Administrative Instructions and must be examined in this case. Thus, claims 5-8, 11, 14, 15, 22-24, 29, 30 and 40-49 should all be examined in this case.

The other claims which have not been deleted without prejudice toward the continuation of prosecution thereof in a divisional application should also be examined in this case as they are all related to the special technical feature of the novel B1 protein of the present invention, and it would not be unduly burdensome to search all of these claims.

With respect to the species election requirement, it should be noted that, in view of the rewriting of the protein and DNA claims to define analogs as comprising no more than ten deletions, substitutions or additions of a single amino acid, the analogs and the functional derivatives (as defined on page 31 of the specification as excluding derivatives that change one amino acid to another) cannot be considered to be patentably distinct from the protein and fragments. Insofar as the examiner's species requirement for Groups IV and V, the claims have been amended to eliminate the terms between which the examiner requires restriction. These claims are now directed to "the modulation of the effect on cells of the B1 polypeptide of SEQ ID NO:1". To the extent an election is still required, applicants elect inflammation. To the extent Group VI remains in this case, applicants elect extracellular application. To the extent Groups IX and XIX remain in the case, applicants elect the CARD domains. To the extent Groups XIV-XVII remain in the case, applicants elect treating a

pathological condition, and to the extent that Group XVIII remains in the case, applicants elect the whole-length B1. It is understood, however, with respect to the election of species, that once a generic claim is found to be allowable that all the species will be examined in this case.

Accordingly, reconsideration and withdrawal of this restriction and examination on the merits of all the claims now present in the case, and particularly claims 5-8, 11, 14, 15, 22-24, 29, 30 and 40-49, are hereby earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

Respectfully submitted,

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Version with Markings to Show Changes Made

Delete claims 1-4, 9, 10, 13, 18, 20, 21, 25-28, 38 and 39.

Add new claims 40-50.

Amend claims 5, 11, 12, 14-17, 19, 22-24 and 29-37.

5 (Amended). A vector comprising a DNA sequence according to claim ~~1~~44.

11 (Amended). A method for producing a ~~B-1 protein, isoform, fragment, analog or derivative thereof according to claim 9 or 10~~polypeptide which directly or indirectly potentiates cell death, which comprises growing a transformed host cell according to claim 8 under conditions suitable for the expression of ~~said protein, isoform, fragment, analog or derivative thereof~~an expression product, effecting post-translational modification of said expression product, as necessary, for obtaining said ~~protein, isoform, fragment, analog or derivative thereof~~polypeptide, and isolating said expressed polypeptide~~protein, isoform, fragment, analog or derivative~~.

12 (Amended). Antibodies or active fragments or derivatives thereof, specific for ~~the B1 protein, isoform, analog, fragment or derivative thereof~~a polypeptide according to claim ~~9~~40.

14 (Amended). A method according to claim ~~13~~49, wherein said treating of cells comprises introducing into said cells a DNA sequence encoding said ~~B1 protein, isoform, fragment, analog or derivative~~ polypeptide in the form of a

suitable vector carrying said sequence, said vector being capable of effecting the insertion of said sequence into said cells in a way that said sequence is expressed in said cells.

15 (Amended). A method according to claim ~~13 or~~ 14, wherein said treating of said cells ~~is by transfection of said cells with a recombinant animal virus vector comprising the steps of~~comprises:

(a) constructing a recombinant animal virus vector carrying a sequence encoding a viral surface protein (ligand that is capable of binding to a specific cell surface receptor on the surface of said cells to be treated and a second sequence encoding ~~a protein selected from said B1 protein, isoforms, analogs, fragments and derivatives according to claim 9 or claim 10, that when expressed in said cells is capable of modulating/mediating the activity of the inflammation, cell death or cell survival pathways, directly or indirectly, or any other intracellular signaling activity modulated/mediated by other intracellular molecules with which said B1 protein, isoforms, analogs, fragments and derivatives interact directly or indirectly~~ said polypeptide; and

(b) infecting said cells with said vector of (a).

16 (Amended). A method for modulating the ~~inflammation, cell death or cell survival pathways in cells which are modulated directly or indirectly by~~ effect on cells of the B1 protein of SEQ ID NO:1, comprising treating said cells with antibodies or active fragments or derivatives thereof, according to claim 12, said treating being by

application to said cells of a suitable composition containing said antibodies, active fragments or derivatives thereof ~~to said cells~~, wherein when ~~the~~ said B1 protein ~~or portions thereof~~ of said cells ~~are~~ is exposed on the extracellular surface, said composition is formulated for extracellular application, and when said B1 ~~proteins are~~protein is intracellular, said composition is formulated for intracellular application.

17 (Amended). A method for modulating the ~~inflammation, cell death, cell survival or other pathways in cells which are modulated directly or indirectly by B1~~effect on cells of the B1 protein of SEQ ID NO:1, comprising treating said cells with an oligonucleotide sequence encoding an antisense sequence ~~for~~ of at least part of ~~the DNA~~a mRNA sequence encoding ~~a~~ said B1 protein ~~according to claim 1~~, said oligonucleotide sequence being capable of blocking the expression of ~~the~~ said B1 protein.

19 (Amended). A method for modulating the ~~inflammation, cell death or cell survival or other pathways in which cells are modulated directly or indirectly by B1~~effect on cells of the B1 protein of SEQ ID NO:1, comprising applying the ribozyme procedure in which a vector encoding a ribozyme sequence capable of interacting with a cellular mRNA sequence encoding a B1 protein ~~according to claim 9~~of SEQ ID NO:1 is introduced into said cells in a form that permits expression of said ribozyme sequence in said cells, and wherein when said ribozyme sequence is expressed in said cells it interacts with

said cellular mRNA sequence and cleaves said mRNA sequence resulting in the inhibition of expression of said B1 protein in said cells.

22 (Amended). A pharmaceutical composition for the modulation of the inflammation, cell death, cell survival or other pathways in cells which are modulated directly or indirectly by the B1 protein of SEQ ID NO:1, comprising a pharmaceutically acceptable excipient and, as active ingredient, at least one ~~B1 protein~~polypeptide~~,~~ according to claim ~~9, its biologically active fragments, analogs, derivatives or mixtures thereof~~40.

23 (Amended). A pharmaceutical composition for the modulation of inflammation, cell death, cell survival or other pathways in cells which are modulated directly or indirectly by the B1~~,~~ protein of SEQ ID NO:1, comprising a pharmaceutically acceptable excipient and, as active ingredient, a recombinant animal virus vector encoding a protein capable of binding a cell surface receptor and encoding ~~at least one B1 protein, isoform, active fragments or analogs,~~said polypeptide according to claim ~~9~~40.

24 (Amended). A pharmaceutical composition for modulating the inflammation, cell death, cell survival or other pathways in cells which are modulated directly or indirectly by the B1 protein of SEQ ID NO:1, comprising a pharmaceutically acceptable excipient and, as active ingredient, an oligonucleotide sequence encoding an ~~anti-sense~~antisense sequence of at least part of a mRNA sequence

encoding of the B1 protein mRNA sequence, according to claim ~~1~~40.

29 (Amended). A method of modulating ~~apoptopic~~ apoptotic processes or programmed cell death processes (cell death pathways) in which the B1 protein of SEQ ID NO:1 is involved directly or indirectly, comprising treating said cells with one or more ~~B1 proteins, isoforms, analogs, fragments or derivatives,~~polypeptide according to claim ~~9~~40, wherein said treating of said cells comprises introducing into said cells said one or more ~~B1 proteins, isoforms, analogs, fragments or derivatives~~polypeptide in a form suitable for intracellular introduction thereof, or introducing into said cells a DNA sequence encoding said one or more ~~B1 proteins, isoforms, analogs, fragments or derivatives~~ polypeptide in the form of a suitable vector carrying said sequence, said vector being capable of effecting the ingestion of said sequence into said cells in a way that said sequence is expressed in said cells.

30 (Amended). A method of modulating cell survival processes in which the B1 protein of SEQ ID NO:1 is involved directly or indirectly and which include the modulation of cell survival, comprising treating said cells with one or more ~~B1 proteins, isoforms, analogs, fragments or derivatives,~~polypeptide according to claim ~~9~~40, wherein said treating of cells comprises introducing into said cells said one or more ~~B1 proteins, isoforms, analogs, fragments or derivatives~~polypeptide in a form suitable for intracellular

introduction thereof, or introducing into said cells a DNA sequence encoding said one or more polypeptide~~B1 proteins, isoforms, analogs, fragments or derivatives~~ in the form of a suitable vector carrying said sequence, said vector being capable of effecting the insertion of said sequence into said cells in a way that said sequence is expressed in said cells.

31 (Amended). A method for screening of a ligand capable of binding to a ~~B1 protein~~polypeptide according to claim ~~9~~40, comprising contacting an affinity chromatography matrix to which said ~~protein~~ polypeptide is attached with a cell extract whereby the ligand is bound to said matrix, and eluting, isolating, ~~and~~ analyzing and producing said ligand.

32 (Amended). A method for screening of a DNA sequence coding for a ligand capable of binding to a ~~B1 protein~~polypeptide according to claim ~~9~~40, comprising applying the yeast two-hybrid procedure in which a sequence encoding said ~~B1 protein~~polypeptide is carried by one hybrid vector and sequences from a cDNA or genomic DNA library are carried by the second hybrid vector, transforming yeast host cells with said vectors, isolating the positively transformed cells, ~~and~~ extracting said second hybrid vector to obtain a sequence encoding said ligand, and identifying and producing said ligand.

33 (Amended). A method for identifying and producing a ligand capable of modulating the cellular activity modulated~~/~~ or mediated by the B1 protein of SEQ ID NO:1, comprising:

a) screening for a ligand capable of binding to a polypeptide comprising at least a portion of said B1 protein having at least some of the amino acid residues of ~~B1 depicted in Fig. 3~~SEQ ID NO:1, which include essentially all of the prodomain (or CARD) of said B1 protein;

b) identifying and characterizing a ligand, other than BCL2, TRAF2, or portions of a receptor of the TNF/NGF receptor family or other known proteins having a prodomain (CARD), found by said screening step to be capable of said binding; and

c) producing said ligand in substantially isolated and purified form.

34 (Amended). A method for identifying and producing a ligand capable of modulating the cellular activity modulated or mediated by a ~~B1 protein~~polypeptide according to claim ~~9~~ 40, comprising:

a) screening for a ligand capable of binding to a polypeptide comprising at least the carboxy terminal portion of the B1 sequence ~~depicted in Fig. 3~~of SEQ ID NO:1, including the prodomain (CARD);

b) identifying and characterizing a ligand, other than BCL2, TRAF2, or portions of a receptor of the TNF/NGF receptor family or other known proteins having a prodomain (CARD), found by said screening step to be capable of said binding; and

c) producing said ligand in substantially isolated and purified form.

35 (Amended). A method for identifying and producing a ligand capable of modulating the cellular activity modulated~~/~~ or mediated by the B1 protein, comprising

a) screening for a ligand capable of binding to at least the N-terminal portion of the B1 sequence ~~depicted in Fig. 3~~of SEQ ID NO:1, including substantially all of the kinase domain of B1;

b) identifying and characterizing a ligand, other than BCL2, TRAF2, or portions of a receptor of the TNF/NGF receptor family or other known intracellular modulatory proteins, found by said screening step to be capable of said binding; and

c) producing said ligand in substantially isolated and purified form.

36 (Amended). A method for identifying and producing a molecule capable of directly or indirectly modulating the cellular activity modulated or ~~/~~mediated by the B1 protein of SEQ ID NO:1, comprising:

a) screening for a molecule capable of modulating activities modulated or ~~/~~mediated by said B1 protein;

b) identifying and characterizing said molecule; and

c) producing said molecule in substantially isolated and purified form.

37 (Amended). A method for identifying and producing a molecule capable of directly or indirectly modulating the cellular activity modulated or ~~/~~mediated by a ~~protein~~ polypeptide according to claim ~~9~~40, comprising:

a) screening for a molecule capable of modulating activities modulated or ~~/~~mediated by ~~a protein according to claim 9~~said polypeptide;

b) identifying and characterizing said molecule; and

c) producing said molecule in substantially isolated and purified form.